

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Tagg *et al.*
U.S. Serial No. : 10/564,799
For : Treatment of Malodour
Filing Date : January 13, 2006
Examiner : C.R. Tate
Art Unit : 1655
Confirmation No. : 3344

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745 Fifth Avenue
New York, NY 10151

DECLARATION UNDER 35 USC § 1.132

Dear Sir:

I, John Robert Tagg, do hereby declare and state that:

1. I am correctly named as a co-inventor on the above-identified patent application (USSN 10/564,799; "the '799 application").
2. I am a Professor of Microbiology at the University of Otago, Leith Street, Dunedin, New Zealand. I am a scientific consultant to Blis Technologies Limited and my brief curriculum vitae is attached as Exhibit 1.
3. I am familiar with the '799 application and July 10, 2008 Office Action. I am also familiar with each of the citations WO 01/27143, Huatan, Chikindas and Kross referred to in that Office Action.
4. I am correctly named as a co-inventor on WO 01/27143.
5. Prior to the present invention as claimed in the '799 application, it was unknown to those of skill in the art that *S. salivarius* bacteriocin like inhibitory substance (BLIS)-producing organisms were capable of acting against bacteria capable of causing halitosis.

6. Prior to the present invention it is my opinion that it was commonly understood by those of skill in the art that bacteriocin producing *S. salivarius* would act against only closely related gram positive bacteria. This is evident from the data provided in WO 01/27143.

7. WO 01/27143 is directed to the *Streptococcus salivarius* strains K12 and K30 and their use to inhibit growth of harmful streptococcal bacteria in the upper respiratory tract including the mouth. The conditions exemplified for treatment include streptococcal sore throats (caused mainly by *S. pyogenes*).

8. *S. pyogenes* is a gram-positive bacteria closely related to *S. salivarius*, and having similar metabolism thereto. Activity of *S. salivarius* against this closely related streptococcus accords with my earlier view that bacteriocins from *S. salivarius* will act against only closely related gram positive bacteria.

9. Based on my knowledge of *S. salivarius* strains, it was entirely unexpected to me to find that in *in vitro* experiments BLIS-producing *S. salivarius* were active against quite unrelated bacteria occupying a different functional niche, particularly bacteria selected from Eubacterium, and Micromonas species and anaerobic gram-negative black-pigmented species (including Prevotella), and especially those producing volatile sulphur compounds.

10. Based on this surprising finding I considered it might be feasible to use *S. salivarius* in treating or preventing halitosis caused by these bacteria.

11. To confirm that hypothesis my co-inventor and I needed to determine if the *S. salivarius* inhibitory activity observed *in vitro* could translate into halitosis treatment *in vivo*.

12. To determine the therapeutic potential of *S. salivarius in vivo* we needed to determine whether the *S. salivarius* could be effective to treat halitosis.

13. My research, and that of my co-inventor, determined halitosis treatment could indeed be effected using BLIS-producing *S. salivarius*.

14. WO 01/27143 states only the use of BLIS-producing *S. salivarius* against closely related gram positive bacteria. Halitosis treatment is not mentioned in that document. Treatment of unrelated organisms such as black-pigmented gram-negative species, Eubacterium and Micromonas species is not mentioned in that document. WO 01/27143 therefore does not teach or suggest the use of BLIS-producing *S. salivarius* strains to treat halitosis.

15. It is my opinion based on my long experience that one of ordinary skill in the art would not be taught by WO 01/27143 that halitosis caused by the unrelated organisms identified above could be treated.

16. Huatan et al. (US 2001/0043941) is directed to providing oral formulations (animal chews) which obviate the need for invasive manipulation of an animal's mouth (especially dogs and cats). Reference to nisin and other lantibiotics as medicaments for local delivery pertinent to oral health is included. However, there is no discussion of delivery of a BLIS-producing bacterium to provide treatment of halitosis.

17. No examples are provided of nisin or lantibiotic being used in the animal chews to effectively treat any oral health condition, let alone halitosis specifically.

18. A bacterium which produces a BLIS active against halitosis causing bacteria is required to provide on-going release of the active from the bacterium into the oral cavity to treat halitosis.

19. Huatan does not teach or suggest the use of BLIS-producing *S. salivarius* (or any organism) for use in the oral cavity to treat halitosis caused by unrelated organisms.

20. Moreover, based on my long experience in this art I would not be motivated to read Huatan together with WO 01/27143. Huatan solves a different problem of how to produce an animal chew to deliver known oral health compounds to pets. That in my view is an unrelated art to the invention. It is not concerned with the benefits of using bacteria to treat halitosis.

21. Chikindas (US 5,672,351) relates to histatin derivatives in the preparation of antimicrobial agents for use in oral care compositions. Other functional biomolecules such as bacteriocins, antibodies and enzymes are mentioned as possible additives. No examples of compositions containing any bacteriocins are provided, nor any bacteriocins identified.

22. Chikindas is directed to control of oral health conditions using a composition containing histatins as active agents. There is no teaching or suggestion of using a BLIS-producing bacterium in the oral cavity and to treat halitosis. Skilled workers are directed to use only isolated active agents which operate by a different mechanism of action.

23. Kross teaches the treatment of oral malodour using chlorite solutions. A pre-conditioning step to produce an acidic environment is used to increase the effectiveness of the chlorite solution.

24. Huatan, Chikindas and Kross are silent on the use of BLIS-producing bacteria to treat halitosis, and do not teach or suggest that such bacteria could be active against unrelated bacteria. This result was entirely surprising to me.

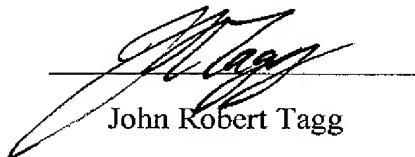
25. In conclusion it is my opinion that the halitosis treatment properties of BLIS-producing *S. salivarius* are entirely unexpected from the teachings in WO 01/27143, Huatan,

Chikindas and Kross. It was very surprising to me, knowing what I do about *S. salivarius*, that the bacteria could be active against bacteria so unrelated to streptococci.

26. In view of the above, I therefore request that the rejections based on WO 01/27143, Huatan, Chikindas and Kross be withdrawn.

27. I hereby state that all statement made herein are of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful and false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such wilful statements my jeopardise the validity of the application or any patent issuing thereon.

3/12/08
Date


John Robert Tagg